

REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the amendments above and comments below.

Claims 1 and 6 are amended to reflect the claims as presented in the allegedly non-compliant Amendment and Response under 37 C.F.R. § 1.116, filed October 20, 2004. Per the Examiner's request in the Advisory Action of November 9, 2004, p. 2, line 7, the claim amendments herein made are with respect to the claims presented in the Response to Notice of Non-Compliant Amendment filed February 13, 2004. No new matter is added by these amendments. The remaining claims 2 and 8-13 are also re-presented as shown in the Response to Notice of Non-Compliant Amendment filed February 13, 2004. Applicants respectfully assert that the foregoing fully addresses the Examiner's formal objections to the Application.

Applicants acknowledge and appreciate the Examiner's withdrawal of the rejection of the claims under 35 U.S.C. §103(a) upon entry of the amendments above. Additionally, Applicants would like to express their appreciation to Examiners Marvich and Leffers for extending Applicants' Representative the courtesy a personal interview on December 21, 2004.

Rejection of Claims 1, 2, 6 and 8-13 und 35 U.S.C. §112, First Paragraph

In the Advisory Action of November 9, 2004, the Examiner argued that the specification does not provide support for the claim term "mature somatotropin". The Examiner's reasoning is set forth in the section entitled "Continuation of 10." Notwithstanding the Examiner's statement in the Advisory Action that Fig. 2 of the specification provides support for porcine mature somatotropin, see p. 2, lines 26-29; the Examiner states that one of skill in the art would not recognize the sequence in Fig. 2 as indicating "that the invention is drawn to the class of somatotropins that are 'mature.'"

At the interview, the Examiners clarified this statement by asserting that although the specification had support for porcine mature somatotropin, the claim term "mature somatotropin" also read on mature somatotropin from many species other than pig.

The case law states that if the skilled artisan would have understood the inventors to be in possession of the claimed invention at the time of filing, then the adequate description requirement is met. *Vas-Cath Inc. v. Mahurkar*, 935 F2d 1555 at 1563 (Fed. Cir. 1991). To this

end, Applicants' representative presented Table 1 of U.S. Patent No. 4,652,630 (Exhibit A; issued March 1987) showing a sequence alignment of mature somatotropins from 5 different species (*i.e.*, bovine, porcine, ovine, avian and human). From Table 1, one of skill in the art would have learned at a minimum, that 1) the sequences of mature somatotropins were well known; 2) all mature somatotropins are about 190 amino acids in length; and 3) somatotropins possessed minimal sequence divergence from bird to human. As such, the skilled artisan would have appreciated that the source of the mature somatotropin used for the cassette of claim 1 is irrelevant and that the recitation "mature somatotropin" would have clearly indicated possession of all mature somatotropins to a person of ordinary skill, at the time of the subject application's filing.

The Examiners agreed with this reasoning. In the Interview Summary, the Examiners stated, "Applicants have provided evidence demonstrating the similarity across species where somatotropin has about 190 amino acids." p. 2, lines 4-5. Notwithstanding this agreement, the Examiners required written memorialization of the foregoing arguments. Applicants respectfully fulfill the Examiners' request herewith.

Remarks Concerning the Claim Recitation "modified insulin secretory signal which has one or more amino acid modifications of the amino acid sequence shown in SEQ ID NO: 1..."

In the interview, the Examiners' attention was drawn to claim 1's recitation "modified insulin secretory signal which has one or more amino acid modifications of the amino acid sequence shown in SEQ ID NO: 1...". The Examiners' felt that the recitation lacked structural guidance as to which amino acids could be altered to retain functionality. Specifically, the Examiner felt that one could modify SEQ ID NO: 1 to ultimately derive a polynucleotide that was anticipated under 35 U.S.C. § 102.

In response to the Examiners' concerns, Applicants respectfully assert that functional insulin secretory signal sequences having amino acid variability were well known at the time of the subject application's filing. Figure 1 of Sures *et al.*, 1980, (Exhibit B) demonstrates that one of skill in the art would have known about structural variability in the well-studied insulin secretory signal by showing the sequence variability present in the human and rat insulin secretory signals (pre-peptide). As such, one of skill in the art would have had an example of

which amino acid residues are amenable to substitution or modification without effecting insulin secretory signal sequence activity.

Furthermore, it is not the amino acid variability in the insulin secretory signal that represents the crux of the invention; rather it is the construction of an expression cassette wherein an insulin secretory signal (regardless which signal sequence variant) is operably linked to a heterologous sequence encoding a mature somatotropin. The Applicants have found that this combination provides *enhanced* secretion of somatotropin. The prior art does not teach or suggest such a combination, let alone any *enhanced* secretion of somatotropin.

CONCLUSION

It is respectfully submitted that the application, as amended above, is in condition for allowance and an early notification thereof is earnestly solicited. To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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